```
=> d his

     (FILE 'HOME' ENTERED AT 19:09:00 ON 03 APR 2002)

     FILE 'CAPLUS' ENTERED AT 19:09:07 ON 03 APR 2002
L1             1 S WO 20000025764/PN
                 SELECT L1 1 RN
L2         42771 S E1-E16
L3          1662 S L2 AND COMBINATION
L4            29 S L3 AND (CARDIOVASCULAR OR HEART)
                 E ATHEROGENIC
                 E ATHEROGENIC DISEASE/CT
                 E E5+ALL
L5         35826 S ARTERIOSCLEROSIS OR ATHEROSCLEROSIS OR THROMBOGENIC
L6         15924 S E6+NT
L7         35826 S L5 OR L6
                 E HYPERHOMCYSTENINEMIA/CT
                 E HYPERHOMOCYSTEINEMIA/CT
                 E HOMOCYSTEINEMIA/CT
L8             0 S TRANSMETHYLATION DISORDER/CT
                 E TRANSMETHYLATION DISORDER/CT
                 E E3+ALL
L9             8 S L3 AND L7
L10        88852 S 107-43-7/RN OR 107-97-1/RN OR DIMETHYGLYCINE OR SARCOSINE OR
L11         2637 S 58-05-9/RN OR 134-35-0/RN OR 2800-34-2/RN OR 3432-99-3/RN OR
                 S 107-43-7/RN OR 107-97-1/RN OR DIMETHYGLYCINE OR SARCOSINE OR

     FILE 'REGISTRY' ENTERED AT 19:25:43 ON 03 APR 2002
L12            1 S 1118-68-9/RN

     FILE 'CAPLUS' ENTERED AT 19:25:43 ON 03 APR 2002
L13          602 S L12
L14        89206 S 107-43-7/RN OR 107-97-1/RN OR DIMETHYGLYCINE OR SARCOSINE OR
L15        15685 S QUERCETIN OR 117-39-5/RN OR BIOFLAVONOID OR ISOQUERCETIN OR Q
L16            1 S L14 AND L15 AND L11
L17          130 S L11 AND L14
L18          102 S L14 AND L15
L19            3 S L11 AND L15
L20           14 S L17 AND COMBINATION

     FILE 'USPATFULL' ENTERED AT 19:34:55 ON 03 APR 2002
L21           82 S L11
L22        27238 S L14
L23         1159 S L15
L24            0 S L21 AND L22 AND L23
L25           31 S L21 AND L22
L26            0 S L21 AND L23
L27          150 S L22 AND L23
L28           21 S L25 AND COMBINATION
L29          127 S L27 AND COMBINATION

=>
```

```
     (FILE 'HOME' ENTERED AT 19:09:00 ON 03 APR 2002)

     FILE 'CAPLUS' ENTERED AT 19:09:07 ON 03 APR 2002
L1             1 S WO 20000025764/PN
                 SELECT L1 1 RN
L2         42771 S E1-E16
L3          1662 S L2 AND COMBINATION
L4            29 S L3 AND (CARDIOVASCULAR OR HEART)
                 E ATHEROGENIC
                 E ATHEROGENIC DISEASE/CT
                 E E5+ALL
L5         35826 S ARTERIOSCLEROSIS OR ATHEROSCLEROSIS OR THROMBOGENIC
L6         15924 S E6+NT
L7         35826 S L5 OR L6
                 E HYPERHOMCYSTENINEMIA/CT
                 E HYPERHOMOCYSTEINEMIA/CT
                 E HOMOCYSTEINEMIA/CT
L8             0 S TRANSMETHYLATION DISORDER/CT
                 E TRANSMETHYLATION DISORDER/CT
                 E E3+ALL

=> s l3 and l7
L9             8 L3 AND L7

=> d ibib abs hitrn l4 1-29

L4   ANSWER 1 OF 29  CAPLUS  COPYRIGHT 2002 ACS
ACCESSION NUMBER:         2001:833015  CAPLUS
DOCUMENT NUMBER:          135:357075
TITLE:                    Compositions containing folic acid and reduced folate
INVENTOR(S):              Haehnlein, Wolfgang; Kraemer, Klaus; Hasselwander,
                          Oliver; Schweikert, Loni
PATENT ASSIGNEE(S):       BASF Aktiengesellschaft, Germany
SOURCE:                   PCT Int. Appl., 19 pp.
                          CODEN: PIXXD2
DOCUMENT TYPE:            Patent
LANGUAGE:                 German
FAMILY ACC. NUM. COUNT:   1
PATENT INFORMATION:

     PATENT NO.        KIND  DATE           APPLICATION NO.  DATE
     --------------    ----  --------       ---------------  --------
     WO 2001084962      A2   20011115       WO 2001-EP4984   20010503
         W:  AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,
             HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS,
             LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO,
             RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ,
             VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
     DE 10022510        A1   20011115       DE 2000-10022510 20000510
PRIORITY APPLN. INFO.:                   DE 2000-10022510 A  20000510
AB   Compns. contg. folic acid in combination with
     5-methyltetrahydrofolic acid are disclosed, as well as compns. contg.
     folic acid, 5-methyltetrahydrofolic acid and/or 5-methyltetrahydrofolic
     acid polyglutamate and a dietary component and/or a dietary prepn. and the
     use thereof.
IT   58-05-9, 5-Formyl-tetrahydrofolic acid 58-05-9D,
     5-Formyl-tetrahydrofolic acid, polyglutamate derivs. 134-35-0,
     5-Methyltetrahydrofolic acid 134-35-0D, glutamates
     2800-34-2, 10-Formyl-tetrahydrofolic acid 2800-34-2D,
     10-Formyl-tetrahydrofolic acid, polyglutamate derivs. 3432-99-3,
```

5,10-Methylene-tetrahydrofolic acid **3432-99-3D**, 5,10-Methylene-tetrahydrofolic acid, polyglutamate derivs. **10360-12-0**, 5,10-Methenyl-tetrahydrofolic acid **10360-12-0D**, 5,10-Methenyl-tetrahydrofolic acid, polyglutamate derivs. **139418-88-5**
RL: FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. contg. folic acid and reduced folate)

L4 ANSWER 2 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:816459 CAPLUS
DOCUMENT NUMBER: 135:339302
TITLE: Methods and compositions for enhancing cellular function through protection of tissue components
INVENTOR(S): Frey, William H., II; Fawcett, John Randall; Thorne, Robert Gary; Chen, Xueqing
PATENT ASSIGNEE(S): Healthpartners Research Foundation, USA
SOURCE: PCT Int. Appl., 77 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001082932	A2	20011108	WO 2001-US13931	20010430
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 2002028786	A1	20020307	US 2001-844450	20010427

PRIORITY APPLN. INFO.:
US 2000-200843P P 20000501
US 2000-230263P P 20000906
US 2000-233025P P 20000915
US 2000-233263P P 20000918

OTHER SOURCE(S): MARPAT 135:339302
AB Methods and compns. for enhancing cellular function through protection of tissue components, such as receptors, proteins, lipids, nucleic acids, carbohydrates, hormones, vitamins, and cofactors, by administering pyrophosphate analogs or related compds. Preferably, the invention provides a method for protecting a muscarinic acetylcholine receptor (mAChR) an/or increasing the efficacy of and agent the directly or indirectly affects a mAChR in a subject in need thereof.
IT **117-39-5**, Quercetin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(methods and compns. for enhancing cellular function through protection of tissue components such as muscarinic receptors by administering pyrophosphate analogs and **combination** with other agents)

L4 ANSWER 3 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:747752 CAPLUS
DOCUMENT NUMBER: 135:303770
TITLE: Preparation of indolin-2-one derivatives and their use as oxytocin receptor ligands
INVENTOR(S): Foulon, Loiec; Garcia, Georges; Serradeil-le Gal, Claudine; Valette, Gerard

PATENT ASSIGNEE(S): Sanofi-Synthelabo, Fr.
SOURCE: PCT Int. Appl., 122 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: French
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

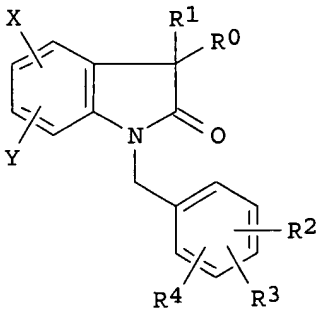
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001074775	A1	20011011	WO 2001-FR980	20010402

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

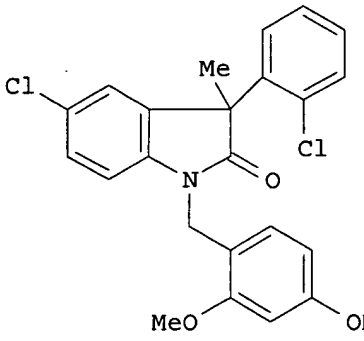
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

FR 2807038	A1	20011005	FR 2000-4193	20000403

PRIORITY APPLN. INFO.: FR 2000-4193 A 20000403
OTHER SOURCE(S): MARPAT 135:303770
GI



I



II

AB Title compds. I [R0 = substituted Ph, pyridyl; R1 = alk(en/yn)yl, alkoxycarbonyl, phenyloxycarbonyl, etc.; R2, R4 = H, Cl, F, alkyl, alkoxy; R3 = Cl, F, alkyl, alkoxy, OH, carbamoyl, alkylcarbonylamino, NO2, CN, etc.; X, Y = H, Cl, Br, I, F, alkoxy, CF3] were prepd. Over 200 examples were prepd. E.g., 5-chloro-3-(2-chlorophenyl)-3-methylindolin-2-one (prepn. given) was treated with t-BuOK in THF @ -40.degree.C, warmed to 0.degree.C and cooled to -60.degree.C. To this cooled mixt. was added a soln. of 2,4-dimethoxyphenylmethanol that was reacted with PBr3 (Et2O, -50.degree.C - 0.degree.C); the resulting soln. warmed to room temp. to give II after work-up. Enantiomers of II were obtained by chiral chromatog. I have affinity for oxytocin receptors (no data) and are used to treat (e.g.) autism, depression, schizophrenia, etc.

IT **1118-68-9**, N,N-Dimethylglycine
RL: RCT (Reactant); RACT (Reactant or reagent)
(reactant; prepn. of indolin-2-one derivs. and their use as oxytocin receptor ligands)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 4 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:703775 CAPLUS

DOCUMENT NUMBER: 135:247229
TITLE: Sugars and amino acids for passage through the blood-brain barrier
INVENTOR(S): Naito, Albert T.
PATENT ASSIGNEE(S): USA
SOURCE: U.S., 6 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6294520	B1	20010925	US 1989-341487	19890327

AB A material which has the ability to effect it's passage, at least in part, and the ability to transport other materials through the blood-brain barrier which includes any one or more pure sugars or pure amino sugars from the group consisting of meso ethritol, xylitol, D(+)galactose, D(+)lactose, D(+)xylose, dulcitol, myo-inositol, L(-)fructose, D(-)mannitol, sorbitol, D(+)glucose, D(+)arabinose, D(-)arabinose, cellobiose, D(+)maltose, D(+)raffinose, L(+)rhamnose, D(+)melibiose, D(-)ribose, adonitol, D(+)arabitol, L(-)arabitol, D(+)fucose, L(-)fucose, D(-)lyxose, L(+)lyxose, L(-)lyxose, D(+)glucosamine, D-mannosamine, and D-galactosamine; and any one or more amino acids from the group consisting of arginine, asparagine, aspartic acid, cysteine, glutamic acid, glycine, histidine, leucine, methionine, phenylalanine, proline, serine, threonine, glutamine, lysine, tryptophan, tyrosine, valine, and taurine. For use in the research or treatment of a subject that material is combined with one or more of the substances beta carotene, xanthophyll, lecithin, calcium, somatostatin, vasopressin, endorphin, enkephalin, acetyl-L-carnitine, GABA, dynorphin, L-tryptophan, choline, thiamine, pyridoxine, niacin, L-arginine, hydroxyproline, NGF, methionine, cystine, potassium, phosphorus, chlorine, sodium, vitamins A, B, C, D and E, and selenium. Thus, **combination** of 0.2-6 g of above sugars and 10-3000 mg of above amino acids and 30 mg beta carotene is used for research or treatment of baldness.

IT **56-45-1**, Serine, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(sugars and amino acids for passage through blood-brain barrier)

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:319728 CAPLUS
DOCUMENT NUMBER: 134:320864
TITLE: High dose folic acid for the treatment of hyperhomocysteinemia
INVENTOR(S): Wilcox, Christopher S.
PATENT ASSIGNEE(S): Cary Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 29 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001030352	A1	20010503	WO 2000-US29788	20001030

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS,

JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-161908P P 19991028

AB Methods are provided for treating patients with hyperhomocysteinemia caused e.g. by end-stage renal disease. The invention also includes related pharmaceutical compns. contg. a folate, vitamins, and other homocysteine-modulating agents which treat severe hyperhomocysteinemia. Specific **combinations** and dosage levels of folic acid and other vitamins are disclosed. These compns. are also contemplated to lessen the incidence and reduce the complications of **cardiovascular** and vascular diseases, and blood coagulation problems assocd. with this group of patients.

IT **56-45-1**, Serine, biological studies **58-05-9**
134-35-0 2800-34-2, 10-Formyltetrahydrofolate
3432-99-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(folic acid for treatment of hyperhomocysteinemia)

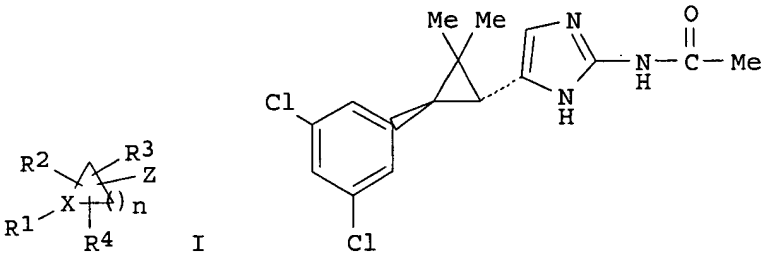
REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 6 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:283949 CAPLUS
DOCUMENT NUMBER: 134:311218
TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors
INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 221 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027107	A2	20010419	WO 2000-US27461	20001002
WO 2001027107	A3	20020124		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-158755P P 19991012
OTHER SOURCE(S): MARPAT 134:311218
GI



I

II

AB Compds. of formula I [wherein; n is 1-5; X is N or CR5, where R5 is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R1 is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R2, R3 and R4 are any of the groups set out for R1 and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R1 is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyldiethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding .alpha.-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical **combinations** are claimed using I and certain antihypertensive agents, .beta.-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

IT **107-97-1**, Sarcosine
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and use of heterocyclic sodium/proton exchange inhibitors)

L4 ANSWER 7 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:247174 CAPLUS
DOCUMENT NUMBER: 134:271267
TITLE: A pharmaceutical composition for stabilising atherosclerotic plaques
INVENTOR(S): Kenton, Kalevi John; Carey, Adam Henry; Carey, Beverly Jane; Haynes, Antony John
PATENT ASSIGNEE(S): Avansis Limited, UK
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001022958	A2	20010405	WO 2000-GB3665	20000925
WO 2001022958	A3	20011115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: GB 1999-22751 A 19990927

AB The invention relates to a pharmaceutical compn. that can be used to treat or prevent disorders of the vascular system. The compn. comprises lycopene in **combination** with a flavonoid, an amino acid, magnesium, ascorbate and vitamin E. Thus, a sachet formulation contained Mg ascorbate 3 and lysine 3 g, vitamin E (emulsified) 300, lycopene 5, and bioflavonoids 600 mg.

IT **153-18-4**, Rutin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical compn. for stabilizing atherosclerotic plaques)

L4 ANSWER 8 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:885381 CAPLUS
DOCUMENT NUMBER: 135:40567
TITLE: Leucovorin and maximum tolerated dose toxicity of methotrexate in rats
AUTHOR(S): Fuskevag, Ole-Martin; Kristiansen, Christel; Lindal, Sigurd; Aarbakke, Jarle
CORPORATE SOURCE: Department of Pharmacology, Institute of Medical Biology, University of Tromso, Tromso, N-9037, Norway
SOURCE: Pediatric Hematology and Oncology (2000), 17(8), 651-658
CODEN: PHONEN; ISSN: 0888-0018
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB High-dose methotrexate (HD-MTX) is widely used in **combination** chemotherapy and can be handled without life-threatening toxicity in **combination** with leucovorin (LV) rescue. However, previous work showed that in an exptl. animal model for testing of short-term HD-MTX effects in anesthetized rats, intolerable toxicity and death occurred within a few hours in some animals. Serum levels were below those routinely found in patients on HD-MTX treatment. This study investigated possible mechanisms for the acute toxicity of MTX in rats. The previously detd. max. tolerated dose of 5 g MTX/kg was used as the test dose. The animals that died showed sudden decreases in **heart** rate and blood pressure. LV, when infused at 1 g/kg immediately prior to MTX, changed the elimination kinetics of MTX, but not its acute toxicity. The data suggest that the acute toxicity of MTX may not be related to its antiproliferative effect, but rather to perturbation of endothelial cell and platelet function.

IT **58-05-9**, Leucovorin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(leucovorin and toxicity of methotrexate)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 9 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:799465 CAPLUS
DOCUMENT NUMBER: 134:80513
TITLE: The flavonoids quercetin and catechin synergistically inhibit platelet function by antagonizing the intracellular production of hydrogen peroxide
AUTHOR(S): Pignatelli, Pasquale; Pulcinelli, Fabio M.; Celestini, Andrea; Lenti, Luisa; Ghiselli, Andrea; Gazzaniga, Pier Paolo; Violi, Francesco
CORPORATE SOURCE: Department of Experimental Medicine and Pathology, Institute of 1st Clinical Medicine, National Institute for Nutrition, University La Sapienza, Rome, 00161, Italy
SOURCE: American Journal of Clinical Nutrition (2000), 72(5),

1150-1155
CODEN: AJCNAC; ISSN: 0002-9165
PUBLISHER: American Society for Clinical Nutrition
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Because it was shown previously that collagen-induced platelet aggregation is assocd. with a burst of hydrogen peroxide, which in turn contributes to stimulating the phospholipase C pathway, this study investigated whether flavonoids synergize in inhibiting platelet function and interfere with platelet function by virtue of their antioxidant effect. The effect of 2 flavonoids, quercetin and catechin, was studied on collagen-induced platelet aggregation and hydrogen peroxide and on platelet adhesion to collagen. Catechin (50-100 .mu.M) and quercetin (10-20 .mu.M) inhibited collagen-induced platelet aggregation and platelet adhesion to collagen. The **combination** of 25 .mu.M catechin and 5 .mu.M quercetin, neither of which had any effect on platelet function when used alone, inhibited collagen-induced platelet aggregation and platelet adhesion to collagen. This **combination** strongly inhibited collagen-induced hydrogen peroxide prodn., calcium mobilization, and 1,3,4-inositol trisphosphate formation. These data indicate that flavonoids inhibit platelet function by blunting hydrogen peroxide prodn. and, in turn, phospholipase C activation and suggest that synergism among flavonoids could contribute to an understanding of the relation between the moderate consumption of red wine and the decreased risk of **cardiovascular** disease.

IT **117-39-5**, Quercetin
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(quercetin and catechin synergistic inhibition of platelet function in relation to effect on hydrogen peroxide prodn.)

REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 10 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:683663 CAPLUS
DOCUMENT NUMBER: 134:173257
TITLE: Is skeletal muscle luxury perfusion the main hemodynamic effect of high-dose insulin in cardiac surgery?
AUTHOR(S): Lindholm, Lena; Nilsson, Boris; Kirno, Klaus; Sellgren, Johan; Nilsson, Folke; Jeppsson, Anders
CORPORATE SOURCE: Department of Cardiothoracic Surgery, Sahlgrenska University Hospital, Goteborg, SE-413 45, Swed.
SOURCE: Scandinavian Cardiovascular Journal (2000), 34(4), 396-402
CODEN: SCJOFY; ISSN: 1401-7431
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Insulin, in **combination** with glucose and potassium (GIK), can be used in **heart** surgery to improve hemodynamic performance. This study evaluates the role of skeletal muscle vasodilation in hemodynamic effects of high-dose GIK therapy early after coronary surgery. Thirty-three male patients undergoing coronary artery bypass grafting were included in a prospective, randomized and controlled study. Eleven patients received infusions of mixed amino acids (11.4 g) and insulin soln. (225 IU insulin, glucose with the glucose clamp technique, and potassium), 11 patients received infusions of mixed amino acids (11.4 g) and 11 patients served as control subjects. During combined insulin and amino acid infusion, cardiac output increased by 13 .+-. 3% (+0.6 .+-. 0.2 L.cntdot.min-1) and systemic vascular resistance decreased by 24 .+-. 3% (-320 .+-. 46 dyn.cntdot.s.cntdot.cm-5). The changes differed from those in the control group (CO:-0.2 .+-. 0.1 L.cntdot.min-1, $p < 0.05$; SVR: +

136 .+-. 42 dyn.cntdot.s.cntdot.cm-5, p < 0.05). Changes in skeletal muscle perfusion and leg vascular resistance did not differ significantly among the groups. At most, changes in leg blood flow could explain 40% of the changes in cardiac output. Skeletal muscle luxury perfusion is not the main hemodynamic effect of high-dose insulin in the early postoperative period after coronary surgery.

IT **56-45-1**, Serine, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(hemodynamic effect of high-dose insulin and mixed amino acid soln. in cardiac surgery)

REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 11 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:568080 CAPLUS
DOCUMENT NUMBER: 134:65951
TITLE: Staril and quercetin **combination** in treatment of conditions of central hemodynamics in patients with congestive **heart** failure
AUTHOR(S): Nurillaeva, N. M.; Gadaev, A. G.; Khurramov, M. O.
CORPORATE SOURCE: Pervyi Tashkent. Gos. Med. Inst., Tashkent, Uzbekistan
SOURCE: Doklady Akademii Nauk Respubliki Uzbekistan (2000), (3), 60-62
CODEN: DARUEE; ISSN: 1019-8954
PUBLISHER: Fan
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB Addn. of the antioxidant quercetin potentiated the pos. effect of ACE inhibitors (Staril) in treatment of congestive **heart** failure.

IT **117-39-5**, Quercetin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Staril and quercetin **combination** in treatment of congestive **heart** failure in patients)

L4 ANSWER 12 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:553409 CAPLUS
DOCUMENT NUMBER: 133:159933
TITLE: L-Arginine based formulations for treating diseases and methods of using same
INVENTOR(S): Kaesemeyer, Wayne H.
PATENT ASSIGNEE(S): Nitrosystems, Inc., USA
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000045809	A1	20000810	WO 2000-US2798	20000204

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1150669 A1 20011107 EP 2000-911701 20000204
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO
PRIORITY APPLN. INFO.: US 1999-118903P P 19990205
WO 2000-US2798 W 20000204

AB A therapeutic mixt. comprised of L-arginine and a nitric oxide synthase agonist (e.g. doxazosin) is disclosed for the treatment of diseases, such as coronary **heart** disease and hypertension.

IT **117-39-5**, Quercetin
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic mixts. contg. doxazosin and nitric oxide synthase substrates for vasodilation)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:251034 CAPLUS
DOCUMENT NUMBER: 133:2790
TITLE: Stat5a serine phosphorylation. Serine 779 is constitutively phosphorylated in the mammary gland, and serine 725 phosphorylation influences prolactin-stimulated in vitro DNA binding activity
AUTHOR(S): Beuvink, Iwan; Hess, Daniel; Flotow, Horst; Hofsteenge, Jan; Groner, Bernd; Hynes, Nancy E.
CORPORATE SOURCE: Friedrich Miescher Institute, Basel, CH-4002, Switz.
SOURCE: Journal of Biological Chemistry (2000), 275(14), 10247-10255
CODEN: JBCHA3; ISSN: 0021-9258
PUBLISHER: American Society for Biochemistry and Molecular Biology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The activity of transcription factors of the Stat family is controlled by phosphorylation of a conserved, carboxyl-terminal tyrosine residue. Tyrosine phosphorylation is essential for Stat dimerization, nuclear translocation, DNA binding, and transcriptional activation. Phosphorylation of Stats on specific serine residues has also been described. We have previously shown that in HC11 mammary epithelial cells Stat5a is phosphorylated on Tyr694 in a prolactin-sensitive manner, whereas serine phosphorylation is constitutive. By using mass spectrometry and site-directed mutagenesis, we have now identified Ser779, located in a unique Stat5a SP motif, as the site of serine phosphorylation. By using phospho-Ser779-specific antiserum, we have detd. that Ser779 is constitutively phosphorylated in mammary glands taken from different developmental stages. Stat5a isolated from spleen, **heart**, brain, and lung was also found to be phosphorylated on Ser779. Ser725 in Stat5a has also been identified as a phosphorylation site. Here we show that mutagenesis of Ser725, Ser779, or a **combination** of Ser725/779 to an Ala had no effect on prolactin-induced transcriptional activation of a .beta.-casein reporter construct. However, following prolactin induction the Ser725 mutant displayed sustained DNA binding activity compared with that of wild type Stat5a. The results suggest that Ser725 phosphorylation has an impact on signal duration.

IT **56-45-1**, L-Serine, biological studies
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(Ser-779, Ser-725; serine 779 of Stat5a is constitutively phosphorylated in mammary gland, and serine 725 phosphorylation influences DNA binding activity)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 14 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:190901 CAPLUS
DOCUMENT NUMBER: 132:227466
TITLE: Oral controlled drug delivery The viscolyzing agent initially and the gel forming polymer thereafter form a hydrated gel matrix which entraps the gas, causing the tablet or capsule to float so that it is retained in the stomach or upper part of the small intestine (spatial control).systems containing swelling agents and polymers
INVENTOR(S): Talwar, Naresh; Sen, Himadri; Staniforth, John H.
PATENT ASSIGNEE(S): Ranbaxy Laboratories Ltd., India
SOURCE: PCT Int. Appl., 57 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015198	A1	20000323	WO 1999-IB78	19990119
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6261601	B1	20010717	US 1998-152932	19980914
AU 9917794	A1	20000403	AU 1999-17794	19990119
EP 1107741	A1	20010620	EP 1999-900106	19990119
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9913696	A	20011009	BR 1999-13696	19990119
NO 2001001276	A	20010510	NO 2001-1276	20010313

PRIORITY APPLN. INFO.:

US 1998-152932	A	19980914
IN 1997-DE2660	A	19970919
WO 1999-IB78	W	19990119

AB A pharmaceutical compn. in th e form of tablets or capsules provides a **combination** of temporal and spatial control of drug delivery to a patient for effective therapeutic results. The pharmaceutical compn. comprises a drug, a gas generating component, a swelling agent, a viscolyzing agent, and optionally a gel forming polymer. The swelling agent belongs to a class of compds. known as superdisintegrants (e.g., crosslinked polyvinylpyrrolidone or sodium CM-cellulose). The viscolyzing agent initially and the gel forming polymer thereafter form a hydrated gel matrix which entraps the gas, causing the tablet or capsule to float so that it is retained in the stomach or upper part of the small intestine (spatial control). At the same time, the hydrated gel matrix creates a tortuous diffusion path for the drug, resulting in sustained release of the drug (temporal control). A preferred once daily ciprofloxacin formulation comprises 69.9% ciprofloxacin base, 0.34% sodium alginate, 1.03% xanthan gum, 13.7% sodium bicarbonate, 12.1% crosslinked polyvinylpyrrolidone, and optionally other pharmaceutical excipients, the formulation being in the form of a coated or uncoated tablet or capsule. Tablets were obtained from Captopril 100.00, Keltrol TF 50.00, Keltrol LVCR 25.00, Avicel PH-102 24.00, Primogel 30.00, NaHCO3 30.00, Mg stearate 3.00, talc and 2.00 mg/tablet.
IT **107-97-1**, Sarcosine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(oral controlled drug delivery systems contg. swelling agents and polymers)
REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 15 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2000:116884 CAPLUS
DOCUMENT NUMBER: 132:146639
TITLE: **Combination** of active substances, especially for the prophylaxis and therapy of ischemic organic lesions and reperfusion syndromes
INVENTOR(S): Nees, Stephan
PATENT ASSIGNEE(S): Vascular Biotech G.m.b.H., Germany
SOURCE: PCT Int. Appl., 37 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000007578	A2	20000217	WO 1999-DE2478	19990806
WO 2000007578	A3	20000511		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9964628	A1	20000228	AU 1999-64628	19990806
EP 1100539	A2	20010523	EP 1999-952335	19990806
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				

PRIORITY APPLN. INFO.: DE 1998-19835674 A 19980806
DE 1998-19844116 A 19980925
WO 1999-DE2478 W 19990806

AB Organ damage, manifested during reperfusion following partial or global ischemia, is prevented or treated by administration of a **combination** of (1) .gtoreq.1 inhibitor of the contractility of venular endothelial cells (VEC) (e.g. a benzopyrone, including flavonoids but excluding anticoagulant benzopyrones such as dicumarol) and (2) .gtoreq.1 cyclooxygenase 1 inhibitor (preferably a NSAID). The **combination** is also useful for treatment of microcirculatory disorders, arteriosclerosis, thrombosis, connective tissue diseases, parodontosis, burns, vasculitis, circulatory shock, eclampsia, etc. Thus, confluent layers of VEC were established on porous filters in an app. for measurement of pressure-sensitive water transport (Lp). Polymorphonuclear leukocytes (PMN) activated with the inflammatory peptide, N-formyl-Met-Leu-Phe, elevated Lp by the VEC by .apprx.300%; this effect was inhibited by apigenin. Simultaneous exposure of VEC to activated PMN and activated blood platelets caused a 1600% elevation in Lp; this effect was totally suppressed by a **combination** of apigenin and acetylsalicylic acid which acted synergistically. The increase in Lp is attributed to release by activated platelets of metabolic precursors which are converted, by interaction with activated PMN, to arachidonic acid metabolites which cause rapid contraction of VEC. The effects on VEC in cell culture were confirmed in expts. on isolated postischemic guinea pig **hearts**. A soln. for organ perfusion was prepd. by adding a lyophilizate contg. trihydroxyethylrutoside 78, acetylsalicylic acid 18, ascorbic acid 18, uric acid 17, inosine 27, aspartic acid 13.3, glutamic

acid 14.6, and arginine 17.4 mg to 1000 mL isotonic soln. buffered to pH 7.4.

IT **117-39-5**, Quercetin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**combination** of active substances for prophylaxis and therapy of ischemic org. lesions and reperfusion syndromes)

L4 ANSWER 16 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:13803 CAPLUS
DOCUMENT NUMBER: 128:93250
TITLE: Compositions and methods for the preservation of living tissue
INVENTOR(S): Wiggins, Philippa M.; Ferguson, Alexander B.
PATENT ASSIGNEE(S): Biostore New Zealand Limited, N. Z.
SOURCE: PCT Int. Appl., 52 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 9
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9747192	A1	19971218	WO 1996-NZ57	19960614
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9661412	A1	19980107	AU 1996-61412	19960614
AU 725247	B2	20001012		
US 5879875	A	19990309	US 1996-662244	19960614
EP 1018866	A1	20000719	EP 1996-918938	19960614
R: CH, DE, FR, GB, LI, SE				
JP 2000512625	T2	20000926	JP 1997-541244	19960614

PRIORITY APPLN. INFO.: WO 1996-NZ57 W 19960614

AB The present invention provides solns. and method for preserving biol. material that enable organs, tissues and cells to be stored for extended periods of time with minimal loss of biol. activity. The inventive solns. may be either (i) substantially isotonic with the biol. material to be preserved and are substantially free of univalent oxyanions and of iodide and/or (ii) comprise a first neutral solute having a mol. wt. of at least about 335 and a soly. in water of at least about 0.3 M, and a second neutral solute having a mol. wt. of less than about 200 and having both hydrophilic and hydrophobic moieties. The inventive solns. preferably contain CaSO4, together with **combinations** of anions and cations from the protein-stabilizing ends of the Hofmeister series, such as K2SO4. The invention also encompasses pretreatment of the biol. material with sodium butyrate prior to the preservation soln. Cultured mouse osteoblasts were dispersed in one of the following solns.; PBS, raffinose/TMAO (1.6:1), raffinose/betaine (1.6:1), trehalose/TMAO (1.6:1), and trehalose/betaine (1.6:1). Osteoblasts survived storage in the inventive solns. for much longer periods than in PBS.

IT **107-43-7**, Betaine **107-97-1**, Sarcosine
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(organ preservation solns. contg. neutral solutes for extended storage)

L4 ANSWER 17 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:771948 CAPLUS
DOCUMENT NUMBER: 128:84142

TITLE: Paclitaxel with mitoxantrone with or without 5-fluorouracil and high-dose leucovorin in the treatment of metastatic breast cancer
AUTHOR(S): Greco, F. Anthony; Hainsworth, John D.
CORPORATE SOURCE: Sarah Cannon-Minnie Pearl Cancer Center, Nashville, TN, 37203, USA
SOURCE: Semin. Oncol. (1997), 24(5, Suppl. 17), 61-64
CODEN: SOLGAV; ISSN: 0093-7754
PUBLISHER: W. B. Saunders Co.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Paclitaxel, administered by 1-h infusion, was added to a previously described **combination** regimen that included mitoxantrone, 5-fluorouracil, and high-dose leucovorin. Patients with metastatic breast cancer received the following regimen as 1st- or 2nd-line treatment: paclitaxel at 135 mg/m2 by 1-h i.v. infusion on day 1; mitoxantrone at 10 mg/m2 by i.v. bolus on day 1; 5-fluorouracil at 350 mg/m2 by i.v. bolus on days 1, 2, and 3; and leucovorin at 300 mg i.v. over 30-60 min, immediately preceding 5-fluorouracil on days 1, 2, and 3. Courses were administered at 3-wk intervals for a total of 8 courses in responding patients. Of 45 assessable patients, 23 (51%) had major responses. Previous chemotherapy, and in particular previous treatment with doxorubicin, did not affect response rate. The median response duration was 7.5 mo. Myelosuppression was moderately severe, with 76% of the courses resulting in grade 3 or 4 leukopenia. There were 4 treatment-related deaths: two from sepsis, one from congestive **heart** failure, and one from sepsis plus congestive **heart** failure, the last two after a large cumulative anthracycline dose. This **combination** regimen was active as 1st- or 2nd-line therapy for metastatic breast cancer, although how its activity compares with that of other **combination** regimens or with paclitaxel alone is unclear. Myelosuppression was more severe than had been anticipated based on previous results with the mitoxantrone/5-fluorouracil/high-dose leucovorin regimen or with single agent paclitaxel administered at this dose and schedule. The infrequent development of cardiotoxicity in these patients suggests that the paclitaxel/mitoxantrone **combination** may not share the problems previously reported with paclitaxel/doxorubicin **combinations**. A phase I/II trial of paclitaxel/mitoxantrone was begun, and the max. tolerated dose was found to be 200 mg/m2 and 10 mg/m2, resp., without the use of cytokines.

IT **58-05-9**, Leucovorin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(breast cancer of humans inhibition by mitoxantrone plus paclitaxel with or without fluorouracil and high-dose)

L4 ANSWER 18 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1997:623049 CAPLUS
DOCUMENT NUMBER: 127:268045
TITLE: Fish oil and garlic nutritive composition
INVENTOR(S): Hsia, Houn Simon; Fan, David
PATENT ASSIGNEE(S): Viva America Marketing, Inc., USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9733599	A1	19970918	WO 1996-US10500	19960617

W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE,

ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG

AU 9662827	A1	19971001	AU 1996-62827	19960617
EP 835119	A1	19980415	EP 1996-921665	19960617
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
CN 1190347	A	19980812	CN 1996-195324	19960617
PRIORITY APPLN. INFO.:			US 1996-25173	19960312
			WO 1996-US10500	19960617

AB The present invention relates to nutritional supplements to the human diet used to increase levels of HDL, and decrease levels of O-LDL, cholesterol, and triglycerides in human blood plasma. More specifically, the present invention teaches a novel nutritional supplements which contain a novel **combination** of fish oil, garlic, rutin, and capsaicin, as well as methods of prepg. the nutritional supplements. A compn. was provided as 2 sep. prepns.; lozenge A contg. 1000 mg fish oil and lozenge B contg. garlic powder 487, capsaicin 53, rutin 27, lemon flavonoid 23, and parsley powder 110 mg. The proper daily dosage was 6 of lozenge A and 4 of lozenge B.

IT **153-18-4**, Rutin
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nutritional supplements contg. fish oils and garlic powders and rutin and capsaicin)

L4 ANSWER 19 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:465191 CAPLUS
DOCUMENT NUMBER: 125:113527
TITLE: Hepatic betaine-homocysteine methyltransferase activity in the chicken is influenced by dietary intake of sulfur amino acids, choline and betaine
AUTHOR(S): Emmert, Jason L.; Garrow, Timothy A.; Baker, David H.
CORPORATE SOURCE: Dep. Anim. Sci., Univ. Illinois, Urbana, IL, 61801, USA
SOURCE: J. Nutr. (1996), 126(8), 2050-2058
CODEN: JONUAI; ISSN: 0022-3166
DOCUMENT TYPE: Journal
LANGUAGE: English

AB There is much interest in the metab. of homocysteine, because elevated plasma homocysteine [hyperhomocyst(e)inemia] is an independent risk factor for the development of **cardiovascular** disease. Four chick assays were conducted to det. the effects of varying dietary sulfur amino acids, choline and betaine on the activity of hepatic betaine-homocysteine methyltransferase (BHMT), an enzyme likely to be important in modulating plasma homocysteine. In Expt. 1, chicks were fed a purified cryst. amino acid diet contg. adequate sulfur amino acids and choline. Excess dietary methionine, or the **combination** of excess cysteine with choline or betaine, caused a small increase ($P < 0.05$) in BHMT activity. In Expt. 2, use of a methionine-deficient purified diet resulted in a threefold increase ($P < 0.05$) in BHMT activity, and addn. of choline or betaine further increased ($P < 0.05$) BHMT activity. In Expt. 3, use of a methionine-deficient corn-peanut meal diet increased BHMT ($P < 0.05$) relative to that of chicks supplemented with adequate methionine, and addn. of surfeit choline to the methionine-deficient basal diet caused a further increase ($P < 0.05$). In Expt. 4, addn. of both surfeit choline and surfeit betaine to the methionine-deficient corn-peanut meal diet caused an increase ($P < 0.05$) in BHMT activity relative to that obsd. in chicks fed the methionine-deficient basal diet. These assays show that large increases in BHMT activity can be produced under methionine-deficient conditions, esp. in the presence of excess choline or

betaine.

IT **107-43-7**, Betaine
RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)
(hepatic betaine-homocysteine methyltransferase activity in the chicken is influenced by dietary intake of sulfur amino acids, choline and betaine)

L4 ANSWER 20 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:316134 CAPLUS
DOCUMENT NUMBER: 125:645
TITLE: Paclitaxel with mitoxantrone, fluorouracil, and high-dose leucovorin in the treatment of metastatic breast cancer: A phase II trial
AUTHOR(S): Hainsworth, John D.; Jones, Stephen E.; Mennel, Robert G.; Blum, Joanne L.; Greco, F. Anthony
CORPORATE SOURCE: Sarah Cannon-Minnie Pearl Cancer Center, Nashville, TN, 37203, USA
SOURCE: J. Clin. Oncol. (1996), 14(5), 1611-1616
CODEN: JCONDN; ISSN: 0732-183X
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Paclitaxel is a highly active single agent in the treatment of breast cancer. However, its optimal incorporation into **combination** regimens awaits definition. In this phase II study, we added paclitaxel, administered by 1-h infusion, to a previously described **combination** regimen that included mitoxantrone, fluorouracil (5-FU), and high-dose leucovorin (NFL). Forty-six patients with metastatic breast cancer received the following regimen as first- or second-line treatment: paclitaxel 135 mg/m2 by 1-h i.v. (IV) infusion on day 1, mitoxantrone 10 mg/ m2 by IV bolus on day 1, 5-FU 350 mg2/m by IV bolus on days 1, 2, and 3, and leucovorin 300 mg IV over 30 to 60 min immediately preceding 5-FU on days 1, 2, and 3. Courses were administered at 3-wk intervals for a total of eight courses in responding patients. Twenty-three of 45 assessable patients (51%) had major responses. Previous chemotherapy, and in particular previous treatment with doxorubicin, did not affect response rate. The median response duration was 7.5 mo. Myelosuppression was moderately severe, with 76% of courses resulting in grade 3 or 4 leukopenia. Hospitalization for treatment of fever during neutropenia was required in 13% of courses, and two patients died as a result of sepsis. Two patients developed severe congestive **heart** failure after a large cumulative anthracycline dose. This **combination** regimen was active as first- or second-line therapy for metastatic breast cancer, although its activity compared with other **combination** regimens or with paclitaxel alone is unclear. Myelosuppression was more severe than anticipated based on previous results with the NFL regimen or with paclitaxel administered at this dose and schedule as a single agent. The infrequent development of cardiotoxicity in these patients suggests that the paclitaxel/mitoxantrone **combination** may not share the problems previously reported with the paclitaxel/ doxorubicin **combination**.

IT **58-05-9**, Leucovorin
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(paclitaxel with mitoxantrone, fluorouracil, and high-dose leucovorin in the treatment of metastatic breast cancer in humans)

L4 ANSWER 21 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1996:150112 CAPLUS
DOCUMENT NUMBER: 124:250023
TITLE: Phase II study of mitoxantrone, 5-fluorouracil, and levo-leucovorin (MLF) in elderly advanced breast cancer patients
AUTHOR(S): Mammoliti, Serafina; Merlini, Laura; Caroti, Cinzia;

Gallo, Luigi
CORPORATE SOURCE: Medical Oncology Dept., Ospedali Galliera, Genoa, Italy
SOURCE: Breast Cancer Res. Treat. (1996), 37(1), 93-6
CODEN: BCTRD6; ISSN: 0167-6806
DOCUMENT TYPE: Journal
LANGUAGE: English

AB We have carried out a phase II trial to evaluate the efficacy and toxicity of a **combination** therapy consisting of mitoxantrone 10 mg/sqm i.v. on day 1, levo-leucovorin 250 mg/sqm administered over 2 h and 5-fluorouracil 500 mg/sqm i.v. push after the first hour of levo-leucovorin infusion, on days 15-16 (MFL) in patients aged more than 65 yr. 24 Patients with advanced breast cancer entered the study: 16 aged 65-70 yrs, 4 patients 70-75 yrs, and 4 > 75 yrs. Median PS was 1 (range 0-2); sites of metastases were: bone 14 patients, viscera 14 patients, soft tissue 11 patients, and CNS 1 patient. A median no. of 6 cycles (range 3-9) was administered. All patients were evaluable for response and toxicity; partial response was obtained in 12 (50%) patients (95% C.I. 30-70), stable disease was obsd. in 9 patients (37.5%), while 3 patients (12.5%) progressed. Median progression-free survival and survival were 9 mo (range 2-14) and 14 mo (range 5-36), resp. Toxicity was generally mild and the most frequently obsd. side-effects were WHO gr. 1-2 leukopenia in 6/24(25%) patients and gr. 1-2 emesis in 10/24 (41.6%) pts. 1 patient pretreated with doxorubicin cumulative dose of 240 mg/sqm showed clin. signs of congestive **heart** failure (NYHA grade 1) after the fifth cycle of treatment. MFL is a well tolerated regimen and could represent a safe and effective treatment in older advanced breast cancer patients.

IT **58-05-9**, Levo-leucovorin
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(phase II study of mitoxantrone, 5-fluorouracil, and levo-leucovorin (MLF) in elderly advanced breast cancer humans)

L4 ANSWER 22 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1995:655227 CAPLUS
DOCUMENT NUMBER: 123:40968
TITLE: **Combination** of sugars with amino acids and other drugs
INVENTOR(S): Naito, Albert
PATENT ASSIGNEE(S): USA
SOURCE: Eur. Pat. Appl., 13 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 652012	A1	19950510	EP 1993-308852	19931105

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

AB A material which has the ability to effect it's passage, at least in part, and the ability to transport other materials through the blood-brain barrier, includes any one or more pure sugars or pure amino sugars from the group consisting of meso-erythritol, xylitol, D-galactose, D-lactose, D-xylose, dulcitol, myo-inositol, L-fructose, D-mannitol, sorbitol, D-glucose, D-(+)-arabinose, D-(-)-arabinose, cellobiose, D-(+)-maltose, D-(+)-raffinose, L-(+)-rhamnose, D-(+)-melibiose, D-(-)-ribose, adonitol, D-(+)-arabitol, L-(-)-arabitol, D-(+)-fucose, L-(-)-fucose, D(-)-lyxose, L-(+)-lyxose, L-(-)-lyxose, D-(+)-glucosamine, D-mannosamine, and D-galactosamine; and any one or more amino acids from the group consisting of arginine, asparagine, aspartic acid, cysteine, glutamic acid, glycine, histidine, leucine, methionine, phenylalanine, proline, serine, threonine,

glutamine, lysine, tryptophan, tyrosine, valine, and taurine. For use in the research or treatment of a subject that material is combined with one or more of the substances .beta.-carotene, xanthophyll, lecithin, calcium, somatostatin, vasopressin, endorphin, enkephalin, acetyl-L-carnitine, GABA, dynorphin, L--tryptophan, choline, thiamine, pyridoxine, niacin, L-arginine, hydroxyproline, NGF, methionine, cystine, potassium, phosphorus, chlorine, sodium, vitamin A, B, C, D and E, tricalcium phosphate, linolenic acid, oats, rice, apple fiber, acidophilus, and selenium.

IT **56-45-1**, Serine, biological studies
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**combination** of sugars with amino acids and drugs for delivery through blood-brain barrier)

L4 ANSWER 23 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1994:124882 CAPLUS
DOCUMENT NUMBER: 120:124882
TITLE: Amines and amine-related derivatives of benzoic acid for treating inflammatory diseases
INVENTOR(S): Shapiro, Howard K.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 89 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9400135	A1	19940106	WO 1993-US6167	19930629
W: AU, BB, BG, BR, CA, CZ, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, SK, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9346553	A1	19940124	AU 1993-46553	19930629
AU 674330	B2	19961219		
EP 604641	A1	19940706	EP 1993-916834	19930629
EP 604641	B1	20020320		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				

PRIORITY APPLN. INFO.: US 1992-906909 A2 19920630
WO 1993-US6167 A 19930629
OTHER SOURCE(S): MARPAT 120:124882
AB Amines capable of covalently binding carbonyl substances, in **combination** with other agents such as antioxidants, free radical scavengers, and vitamins are used for the treatment of chronic inflammatory disorders featuring oxidative free radical reactions, lipid peroxidn., and generation of carbonyl compds. A clin. study showed that an administration of vitamin E 800 IU, methionine 1g, and PABA 1.1g per day to a patient with arthritis decreased pain and improved functional status.

IT **58-05-9**, Folinic acid
RL: BIOL (Biological study)
(chronic inflammatory disease treatment with amines and)

L4 ANSWER 24 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1991:675503 CAPLUS
DOCUMENT NUMBER: 115:275503
TITLE: Branched-chain amino acid transport in cytoplasmic membranes of Leuconostoc mesenteroides subsp. dextranicum CNRZ 1273
AUTHOR(S): Winters, David A.; Poolman, Bert; Hemme, Denis; Konings, Wil N.
CORPORATE SOURCE: Dairy Res. Stn., Inst. Natl. Rech. Agron.,

Jouy-en-Josas, 78352, Fr.
SOURCE: Appl. Environ. Microbiol. (1991), 57(11), 3350-4
CODEN: AEMIDF; ISSN: 0099-2240
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Membrane vesicles of L. mesenteroides dextranicum fused with proteoliposomes prepd. from Escherichia coli phospholipids contg. beef **heart** cytochrome c oxidase were used to study the transport of branched-chain amino acids in a strain isolated from a raw milk cheese. At a medium pH of 6.0, oxidn. of an electron donor system comprising ascorbate, N,N,N',N'-tetramethyl-p-phenylenediamine, and horse **heart** cytochrome c resulted in a membrane potential (.DELTA..psi.) of -60 mV, a pH gradient of -36 mV, and an L-leucine accumulation of 76-fold (.DELTA..mu.Leu/F = 108 mV). Leucine uptake in hybrid membranes in which a .DELTA..psi., .DELTA.pH, Na+ gradient, or a **combination** of these was imposed artificially revealed that both components of the protonmotive force (.DELTA.p) could drive leucine uptake but that a chem. Na+ gradient could not. Kinetic anal. of leucine (valine) transport indicated 3 secondary transport systems with Kt values of 1.7 (0.8) mM, 4.3 (5.9) .mu.M, and 65 (29) nM, resp. L-Leucine transport via the high-affinity leucine transport system (Kt = 4.3 .mu.M) was competitively inhibited by L-valine and L-isoleucine (Ki and Kt values were similar), demonstrating that the transport system translocates branched-chain amino acids. Similar studies with these hybrid membranes indicated the presence of high-affinity secondary transport systems for 10 other amino acids.
IT **56-45-1**, L-Serine, biological studies
RL: BIOL (Biological study)
(transport of, by Leuconostoc mesenteroides dextranicum)

L4 ANSWER 25 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:622368 CAPLUS
DOCUMENT NUMBER: 109:222368
TITLE: Reduction of cellular energy requirements. Screening for agents that may protect against CNS ischemia
AUTHOR(S): Zager, Eric L.; Ames, Adelbert, III
CORPORATE SOURCE: Neurosurg. Serv., Massachusetts Gen. Hosp., Boston, MA, USA
SOURCE: J. Neurosurg. (1988), 69(4), 568-79
CODEN: JONSAC; ISSN: 0022-3085
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Protection of the brain and spinal cord against ischemia is a goal of vast clin. importance. One approach to this objective is to reduce the tissue's functional activity in order to preserve energy for the metabolic processes that are essential to viability. Expts. to explore ways of reducing function-related energy demands were performed on isolated rabbit retina, a well-characterized model of organized adult mammalian central nervous system (CNS) tissue. The retina was maintained in a nearly physiol. state in a miniature **heart**-lung app. Energy metab. (O consumption and glycolysis) and electrophysiol. function (detd. by electroretinogram) of the in vitro retina were monitored, and their responses to a series of agents that may reduce energy requirements were detd. Large reversible redns. in O consumption, glycolysis, and electrophysiol. function were seen in response to mild hypothermia (-3.degree. to -6.degree.), phenytoin (100-200 mg/kg), chlordiazepoxide (200 .mu.M), Li+ (1-4 mM), Mg2+ (6-20 mM), strophanthidin (0.15-0.25 .mu.M), CO2 (25%-30%), 2-amino-5-phosphonovaleric acid (500 .mu.M), amiloride (1 mM), and dantrolene (1 mM). One retina was exposed simultaneously to a **combination** of 6 of these agents, which reduced its oxidative and glycolytic metab. to <50% of the control level. The retina recovered metabolic and electrophysiol. function after a 2.5-h exposure period. Other agents tested (diphenhydramine, midazolam, nifedipine, nimodipine, and quercetin) had effects on energy metab. and electrophysiol. function that were poorly reversible. Surprisingly little

effect was seen in response to general anesthetic agents (thiopental and Althesin) and other CNS depressants (chlorpromazine, EtOH, lidocaine, paraldehyde, valproic acid, and baclofen). The presumed mechanisms through which these agents reduce cellular energy requirements, as well as their potential roles in the treatment of CNS ischemia, are discussed.

IT **117-39-5**, Quercetin
RL: PRP (Properties)
(central nervous system-protective effect of, in ischemia)

L4 ANSWER 26 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1988:490661 CAPLUS
DOCUMENT NUMBER: 109:90661
TITLE: Effect of chronic diabetes on myocardial fuel metabolism and insulin sensitivity
AUTHOR(S): Barrett, Eugene J.; Schwartz, Ronald G.; Young, Lawrence H.; Jacob, Ralph; Zaret, Barry L.
CORPORATE SOURCE: Sch. Med., Yale Univ., New Haven, CT, USA
SOURCE: Diabetes (1988), 37(7), 943-8
CODEN: DIAEAZ; ISSN: 0012-1797
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To assess the effect of chronic insulin-deficient diabetes on myocardial fuel substrate metab. in vivo, the authors measured the myocardial balance of glucose, free fatty acids (FFAs), and amino acids in 9 postabsorptive conscious dogs 4-6 wk after treatment with streptozocin. The acute effect of insulin on the myocardial balance of these same substrates was measured in 6 dogs. Three addnl. dogs were given a const. infusion of amino acids during the insulin clamp to blunt the insulin-induced hypoaminoacidemia. In these dogs, the fasting plasma glucose concn. was markedly elevated. In the basal period, there was no significant glucose uptake by the **heart**; furthermore, physiol. hyperinsulinemia did not stimulate glucose uptake. Postabsorptively, arterial FFAs were elevated in diabetic animals, and there was a significant net extn. of FFAs by the **heart**. During the insulin clamp, arterial FFAs declined, as did **heart** FFA uptake and the net extn. ratio for FFAs was unchanged. Similarly, the arterial branched-chain amino acid (BCAA) concn. was elevated in the postabsorptive state, and there was a significant myocardial uptake of these amino acids and of alanine. With infusion of insulin alone or a **combination** of insulin and amino acids, there was a highly significant linear correlation between the arterial BCAA concn. and myocardial BCAA uptake. Glutamine is the dominant amino acid released by the diabetic myocardium, both in the basal period and during insulin infusion. Thus, when compared with myocardium of normal dogs, the myocardium of diabetic dogs is severely resistant to the action of insulin to promote glucose uptake.

IT **56-45-1**, Serine, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(metab. of, by **heart**, insulin effect on, in diabetes mellitus)

L4 ANSWER 27 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:561484 CAPLUS
DOCUMENT NUMBER: 107:161484
TITLE: Study of chemical substances of Viola tricolor L
AUTHOR(S): Papay, Valeria; Molnar, Bela; Lepran, Istvan; Toth, Laszlo
CORPORATE SOURCE: Gyogynoveny- Drogismereti Intez., SZOTE, Szeged, 6720, Hung.
SOURCE: Acta Pharm. Hung. (1987), 57(3-4), 153-8
CODEN: APHGAO; ISSN: 0001-6659
DOCUMENT TYPE: Journal
LANGUAGE: Hungarian

AB Five flavonoids, 2 salicylic acid derivs., 4 terpenes and triterpenes resp., a mixt. of steroids, carbohydrate derivs., a polysaccharide and Mg

tartrate were isolated and identified from the aerial part of V. tricolor. From the petroleum ether ext. of the herb a lot of fatty acids among them vitamin F were identified by gas chromatog./mass spectrometry. Free and bound amino acids and amino acid compn. of mucilage were detd. by amino-acid analyzer. Mucilage contents were quantified gravimetrically and the total flavonoid contents spectrophotometrically. V. tricolor In **combination** with other medicinal plants may be effective in prevention of **heart** infarction because of its content of flavonoids, unsatd. fatty acids, Mg salts and mucilage. It can be applied in pharmaceutical as well as cosmetic prepns. and because of its anti-inflammatory effect it can be used with good results.

IT **153-18-4**, Rutin
RL: BIOL (Biological study)
(of Viola tricolor, pharmacol. activity in relation to)

L4 ANSWER 28 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1981:584306 CAPLUS
DOCUMENT NUMBER: 95:184306
TITLE: Conditioned cardiac response to the olfactory stimuli of amino acids in the channel catfish, Ictalurus punctatus
AUTHOR(S): Little, Edward E.
CORPORATE SOURCE: Dep. Biol. Sci., Florida State Univ., Tallahassee, FL, 32306, USA
SOURCE: Physiol. Behav. (1981), 27(4), 691-7
CODEN: PHBHA4; ISSN: 0031-9384
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The channel catfishes behavioral sensitivity to amino acids was detd. by monitoring their **heart** rate during the presentation of shock-paired amino acid solns. The response, a deceleration in the **heart** rate, was mediated through olfaction. After limited training, catfish responded to 17 different amino acids. Threshold concns. of 10-9M cysteine or alanine, 10-8M glutamine, and 10-8M serine were found. Quant. differences in the magnitude of response evoked by different amino acids were obsd. Fish trained to respond to a particular amino acid tended to generalize their response to novel amino acids. However, the fish were easily trained to discriminate between different amino acids. Simple mixts. of 2 amino acids were discriminated from the single amino acid components, suggesting that the **combination** of amino acids results in a uniquely different olfactory stimulus.

IT **56-45-1**, biological studies
RL: PRP (Properties)
(odor of, **heart** conditioned reflex redn. by, in channel catfish)

L4 ANSWER 29 OF 29 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1970:400951 CAPLUS
DOCUMENT NUMBER: 73:951
TITLE: Flavonoid distribution in Juglans regia
AUTHOR(S): Spiegl, P.; Chirikdjian, J. J.
CORPORATE SOURCE: Pharm. Inst., Univ. Wien, Vienna, Austria
SOURCE: Pharmazie (1969), 24(12), 780-1
CODEN: PHARAT
DOCUMENT TYPE: Journal
LANGUAGE: German

AB The leaves of J. regia (walnut) are known to contain 2 flavonoids (K. Herrmann, 1955). By using thin-layer chromatog. on a cellulose layer, 10 flavonoids (including their glycosides) could be shown present in various **combinations** in different plant parts (leaf, branch bark, trunk bark without borke (cork), borke (cork), sap wood, **heart** wood). Two-dimensional chromatog. was used, with 60% AcOH for one direction and 15% AcOH for the other. The flavonoids were mostly of the quercetin (I) series, chiefly present as glycosides On hydrolyzing in 2N HCl, 2 hr, the

chief aglycons obtained were I and kaempferol. The chief glycosides present were the 3-rhamnoside of I (quercitrin) (II) and the 3-galactoside of I (hyperoside) (III). Two spots could not be identified due to insufficient pure material; these appeared to be arabinosides of I. The various plant parts all contained four or more flavonoids, except the **heart** wood (III only). Spectral data and breakdown reactions are reported in detail for II and III.

IT **482-36-0**
RL: BOC (Biological occurrence); BIOL (Biological study); OCCU (Occurrence)
(of Juglans regia)

=>

```
> d sel
E1              1       10360-12-0/BI
E2              1       107-43-7/BI
E3              1       107-97-1/BI
E4              1       1118-68-9/BI
E5              1       117-39-5/BI
E6              1       134-35-0/BI
E7              1       139418-88-5/BI
E8              1       153-18-4/BI
E9              1       20229-56-5/BI
E10             1       2800-34-2/BI
E11             1       3432-99-3/BI
E12             1       482-35-9/BI
E13             1       482-36-0/BI
E14             1       491-50-9/BI
E15             1       56-45-1/BI
E16             1       58-05-9/BI
```

research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * * *

FILE 'HOME' ENTERED AT 17:36:12 ON 21 DEC 2001

=> file reg
COST IN U.S. DOLLARS

	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	0.15	0.15

FILE 'REGISTRY' ENTERED AT 17:36:25 ON 21 DEC 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

STRUCTURE FILE UPDATES: 20 DEC 2001 HIGHEST RN 377724-19-1
DICTIONARY FILE UPDATES: 20 DEC 2001 HIGHEST RN 377724-19-1

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

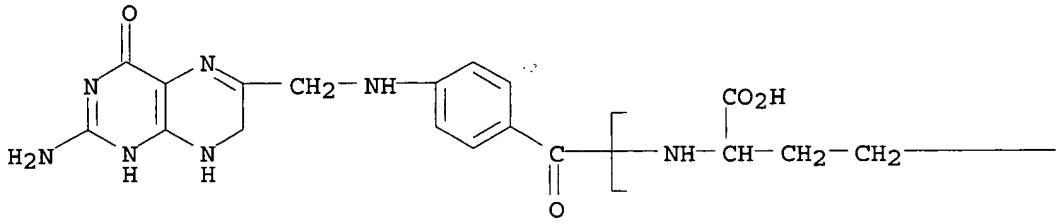
Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

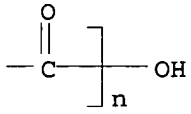
Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

```
=> s dihydrofolic acid
            11 DIHYDROFOLIC
       5212123 ACID
          7693 ACIDS
       5217731 ACID
                (ACID OR ACIDS)
L1          11 DIHYDROFOLIC ACID
                (DIHYDROFOLIC(W)ACID)

=> d l1 1-11

L1   ANSWER 1 OF 11  REGISTRY  COPYRIGHT 2001 ACS
RN   87404-63-5  REGISTRY
CN   Poly[imino(1-carboxy-4-oxo-1,4-butanediyl)],
.alpha.-[4-[[(2-amino-1,4,7,8-
     tetrahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-.omega.-hydroxy-,
(S)-
     (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   Dihydrofolic acid polyglutamate
MF   (C5 H7 N O3)n C14 H14 N6 O3
CI   PMS
PCT  Polyamine
LC   STN Files:   CA, CAPLUS, TOXCENTER, TOXLIT
```

PAGE 1-A



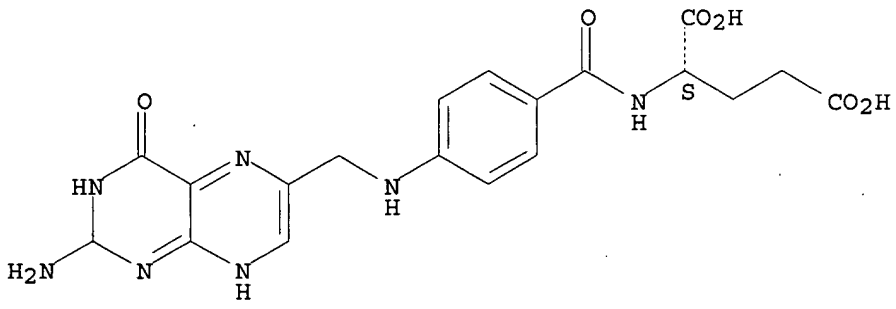
PAGE 1-B



4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 83961-83-5 REGISTRY
CN L-Glutamic acid, N-[4-[[(2-amino-1,2,3,4-tetrahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **1,2-Dihydrofolic acid**
FS STEREOSEARCH
MF C19 H21 N7 O6
LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.

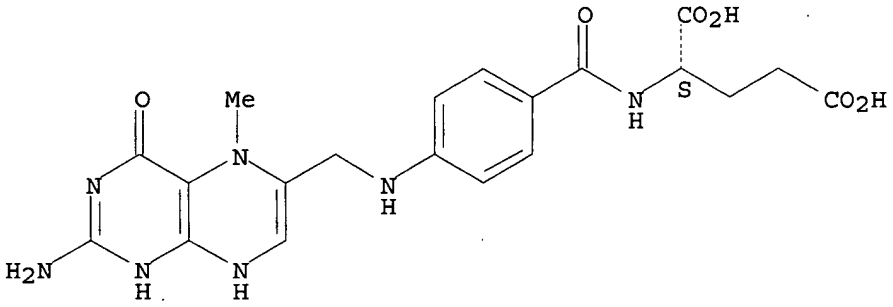


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 59904-24-4 REGISTRY
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,8-tetrahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, N-[p-[[(2-aminodihydro-4-hydroxy-5-methyl-6-pteridinyl)methyl]amino]benzoyl]- (7CI)
OTHER NAMES:
CN **5-Methyl-5,8-dihydrofolic acid**
FS STEREOSEARCH
MF C20 H23 N7 O6
LC STN Files: CA, CAOLD, CAPLUS, MEDLINE, TOXLIT

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

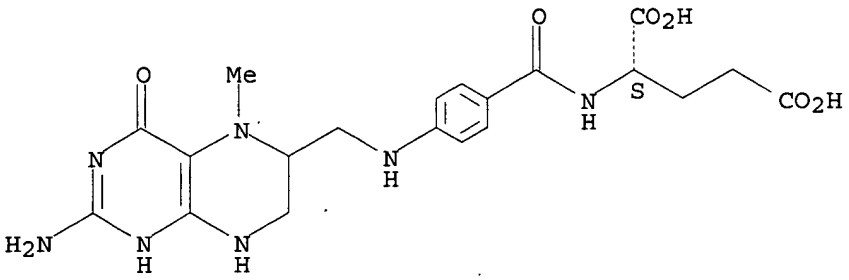
4 REFERENCES IN FILE CA (1967 TO DATE)
4 REFERENCES IN FILE CAPLUS (1967 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 59299-76-2 REGISTRY
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,6,7,8-hexahydro-5-methyl-4-oxo-6-pteridinyl)methyl]amino]benzoyl]-, didehydro deriv. (9CI) (CA INDEX NAME)
OTHER NAMES:
CN **N5-Methyldihydrofolic acid**
FS STEREOSEARCH
MF C20 H23 N7 O6
CI IDS
LC STN Files: CA, CAPLUS

CM 1

CRN 134-35-0
CMF C20 H25 N7 O6

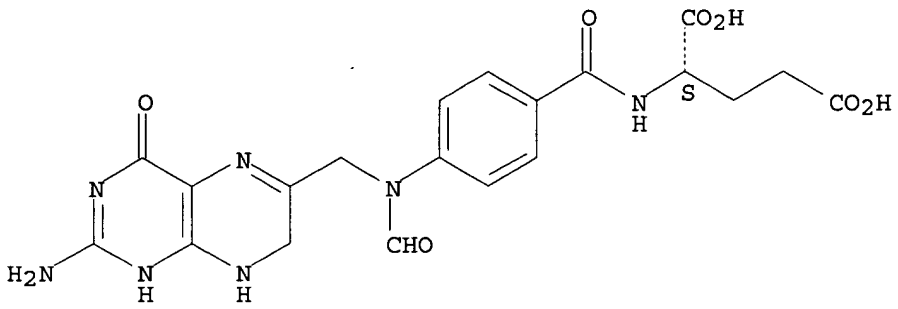
Absolute stereochemistry.



5 REFERENCES IN FILE CA (1967 TO DATE)
5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 28459-40-7 REGISTRY
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,7,8-tetrahydro-4-oxo-6-pteridinyl)methyl]formylamino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, N-[p-[N-[(2-amino-7,8-dihydro-4-hydroxy-6-pteridinyl)methyl]formamido]benzoyl]- (8CI)
OTHER NAMES:
CN **N-Formyl-7,8-dihydrofolic acid**
FS STEREOSEARCH
MF C20 H21 N7 O7
CI COM
LC STN Files: BEILSTEIN*, CA, CANCERLIT, CAPLUS, MEDLINE, TOXCENTER, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

8 REFERENCES IN FILE CA (1967 TO DATE)
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
8 REFERENCES IN FILE CAPLUS (1967 TO DATE)

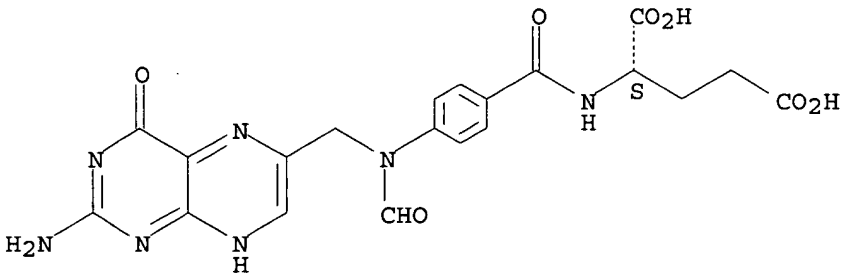
L1 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 25377-55-3 REGISTRY
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,?,?-tetrahydro-4-oxo-6-pteridinyl)methyl]formylamino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, N-[p-[N-[(2-aminodihydro-4-hydroxy-6-pteridinyl)methyl]formamido]benzoyl]-, L- (8CI)

OTHER NAMES:
CN **10-Formyldihydrofolic acid**
CN **N10-Formyldihydrofolic acid**
FS STEREOSEARCH
DR 35-76-7
MF C20 H21 N7 O7
CI IDS
LC STN Files: AGRICOLA, BIOSIS, CA, CAPLUS, DDFU, DRUGU, NIOSHTIC, TOXCENTER, TOXLIT

CM 1

CRN 134-05-4
CMF C20 H19 N7 O7

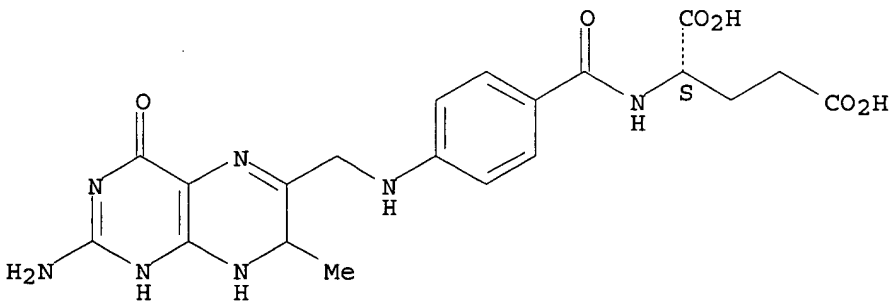
Absolute stereochemistry.



22 REFERENCES IN FILE CA (1967 TO DATE)
22 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 17138-86-2 REGISTRY
CN Glutamic acid, N-[p-[[(2-amino-7,8-dihydro-4-hydroxy-7-methyl-6-pteridinyl)methyl]amino]benzoyl]-, L- (8CI) (CA INDEX NAME)
OTHER NAMES:
CN **7-Methyl-7,8-dihydrofolic acid**
CN **C7-Methyldihydrofolic acid**
FS STEREOSEARCH
MF C20 H23 N7 O6
LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT
(*File contains numerically searchable property data)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

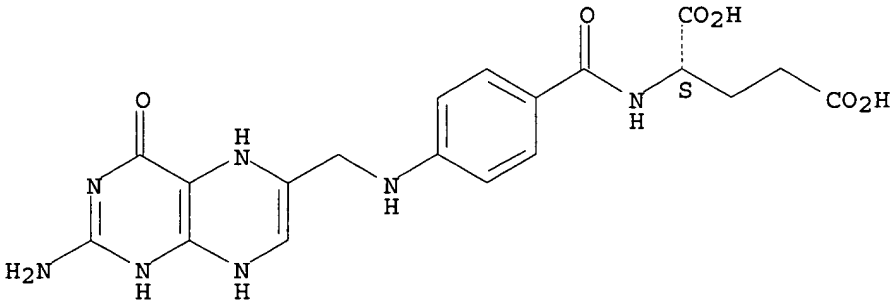
3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 9002-03-3 REGISTRY
CN Dehydrogenase, tetrahydrofolate (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7,8-Dihydrofolate reductase
CN Dihydrofolate dehydrogenase
CN Dihydrofolate reductase
CN **Dihydrofolic acid reductase**
CN Dihydrofolic reductase
CN Dihydropteroylglutamate reductase
CN E.C. 1.5.1.3
CN E.C. 1.5.1.4
CN Folate reductase
CN Folic acid reductase
CN Folic reductase
CN NADP-dihydrofolate reductase
CN NADPH-dihydrofolate reductase
CN Reductase, dihydrofolate
CN Tetrahydrofolate dehydrogenase
DR 9001-17-6, 9038-35-1
MF Unspecified
CI MAN
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CIN, EMBASE, IFICDB, IFIPAT, IFIUDB, PROMT, TOXCENTER, TOXLIT, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
4287 REFERENCES IN FILE CA (1967 TO DATE)
309 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
4291 REFERENCES IN FILE CAPLUS (1967 TO DATE)

L1 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 4033-31-2 REGISTRY
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,5,8-tetrahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, N-[p-[[(2-amino-5,8-dihydro-4-hydroxy-6-pteridinyl)methyl]amino]benzoyl]- (7CI, 8CI)
OTHER NAMES:
CN **5,8-Dihydrofolic acid**
FS STEREOSEARCH
MF C19 H21 N7 O6
LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXLIT
(*File contains numerically searchable property data)

Absolute stereochemistry.

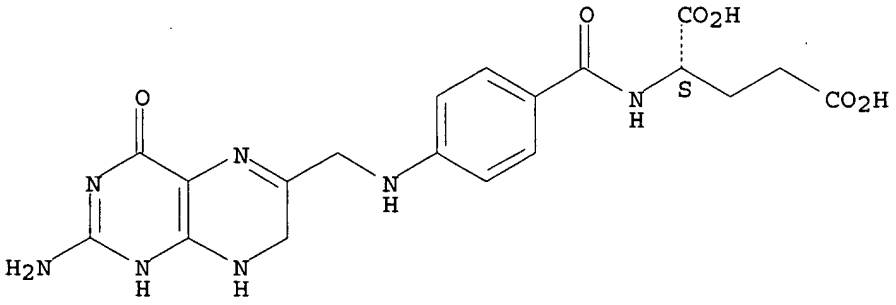


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)
2 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 4033-27-6 REGISTRY
CN L-Glutamic acid, N-[4-[[(2-amino-1,4,7,8-tetrahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, N-[p-[[(2-amino-7,8-dihydro-4-hydroxy-6-pteridinyl)methyl]amino]benzoyl]-, L- (6CI, 7CI, 8CI)
OTHER NAMES:
CN 7,8-Dihydro-L-folic acid
CN **7,8-Dihydrofolic acid**
CN **Dihydrofolic acid**
FS STEREOSEARCH
MF C19 H21 N7 O6
CI COM
LC STN Files: ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, CA, CANCERLIT, CAOLD, CAPLUS, CHEMCATS, DDFU, DRUGU, MEDLINE, TOXCENTER, TOXLIT, USPATFULL
(*File contains numerically searchable property data)

Absolute stereochemistry.



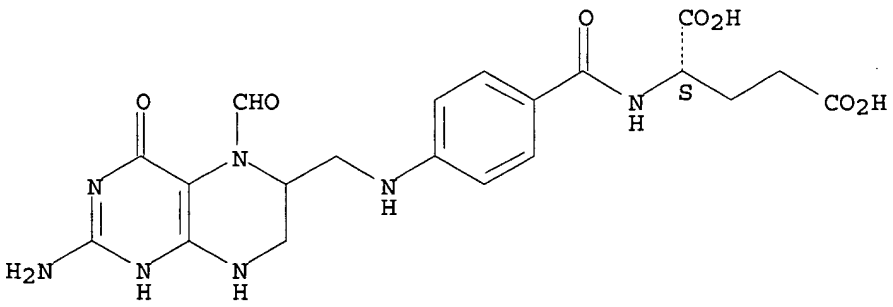
PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

549 REFERENCES IN FILE CA (1967 TO DATE)

23 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
549 REFERENCES IN FILE CAPLUS (1967 TO DATE)
23 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

L1 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2001 ACS
RN 58-05-9 REGISTRY
CN L-Glutamic acid, N-[4-[[(2-amino-5-formyl-1,4,5,6,7,8-hexahydro-4-oxo-6-pteridinyl)methyl]amino]benzoyl]- (9CI) (CA INDEX NAME)
OTHER CA INDEX NAMES:
CN Glutamic acid, N-[p-[[(2-amino-5-formyl-5,6,7,8-tetrahydro-4-hydroxy-6-pteridinyl)methyl]amino]benzoyl]-, L- (8CI)
OTHER NAMES:
CN **10-Formyl-7,8-dihydrofolic acid**
CN 5-Formyl-5,6,7,8-tetrahydrofolic acid
CN 5-Formyltetrahydrofolic acid
CN 5-Formyltetrahydropteroylglutamic acid
CN Folinic acid
CN Folinic acid-SF
CN l-Leucovorin
CN Leucal
CN Leucovorin
CN Levoleucovorin
CN N5-Formyl-5,6,7,8-tetrahydrofolic acid
CN N5-Formyltetrahydrofolic acid
CN Welcovorin
FS STEREOSEARCH
DR 641-41-8, 121521-95-7, 17435-36-8, 3102-53-2, 33299-78-4, 34786-59-9, 40244-99-3
MF C20 H23 N7 O7
CI COM
LC STN Files: ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOBUSINESS, BIOSIS, BIOTECHNO, CA, CABA, CANCERLIT, CAOLD, CAPLUS, CASREACT, CBNB, CHEMCATS, CHEMLIST, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HODOC*, HSDB*, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, NIOSHTIC, PHARMASEARCH, PROMT, TOXCENTER, TOXLIT, USAN, USPATFULL, VETU
(*File contains numerically searchable property data)
Other Sources: EINECS**
(**Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1629 REFERENCES IN FILE CA (1967 TO DATE)
  36 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
1634 REFERENCES IN FILE CAPLUS (1967 TO DATE)
  10 REFERENCES IN FILE CAOLD (PRIOR TO 1967)